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Chlamydia trachomatis Reinfection Rates Among Female Adolescents Seeking Rescreening in School-Based Health Centers

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Abstract

Background—*Chlamydia trachomatis* (CT) infections are common among adolescents attending high and middle schools. The study objective was to determine the reinfection rates of CT for females attending school-based health centers.

Methods—Adolescents attending school-based health centers who reported they were sexually active were screened for CT using nucleic acid amplification tests on cervical or urine samples. Between 1996 and 2003, 10,609 female students were tested. The overall annual prevalence for unduplicated students in a calendar year ranged from 15.1% to 19.5%. Reinfection was defined as a positive test result occurring between 30 and 365 days after an initial positive result.

Results—There were 897 female students who tested positive for CT and returned for at least 1 subsequent test between 30 and 365 days later. Of these, 236 had 1 or more subsequent positive tests for a cumulative incidence of reinfection in 1 year of 26.3% (95% confidence interval = 23.4-29.2%). Young age at first infection was significantly associated with increased risk of subsequent infection (P <0.01). Across sites, the cumulative incidence of reinfection in these female students ranged from 14.3% to 38.9%.

Conclusions—The chlamydia cumulative incidence of reinfection in these female adolescents attending high and middle schools was high and supports the Centers for Disease Control and Prevention recommendation to screen adolescents frequently, especially those with a history of a previous chlamydia infection.

IN THE UNITED STATES, nearly half of high school students (46.8%) have had sexual intercourse.[1] According to the Youth Risk Behavior Surveillance, sexual intercourse increased from 34.3% among ninth graders to 63.1% for twelfth graders; 6.2% initiated sexual activity before the age of 13 years; and 14.3% of students reported ≥4 partners during their lifetime.[1] *Chlamydia trachomatis* (CT) and other sexually transmitted infections (STIs) are prevalent and often asymptomatic among sexually active adolescents.[2-7] Reinfection with chlamydia is also very common and has been previously reported in our schools.[3,4,8-11] Since the newer

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nucleic acid amplification tests (NAATs) can be used with noninvasive specimens such as urine or vaginal swabs, screening adolescents in nontraditional venues, such as school-based health centers (SBHCs) is possible.[12] Use of internet recruitment and mailed specimens is now feasible.[13] We assessed cumulative incidence of chlamydia reinfection in students who were tested more than once within 1 year among adolescent males and females attending SBHCs in Baltimore schools over an 8-year period from a historic surveillance database of NAAT results.

Methods

Students in Baltimore City SBHCs (8 high schools and 3 middle schools) have been screened since 1994 for chlamydia and gonorrhea using NAATs as part of the Centers for Disease Control and Prevention (CDC) funded Infertility Prevention Program. We retrospectively analyzed the deidentified database information for the years 1996-2003 to ascertain the cumulative incidence of chlamydia reinfection over 1 year in female students who were tested more than once within 1 year. Not all students who had an initial positive test presented for a follow-up test. General instructions to users of the SBHCs were for all adolescents who have had a positive chlamydia test to return for retesting at 3 months. All sexually active adolescents who use the SBHCs were requested to report for screening twice a year.

Samples submitted included either cervical or urine samples; the schools switched from cervical samples to urine samples in 1998. All samples were tested by NAATs. Each time students attended the SBHCs, they were asked whether they were sexually active. If they were, they were eligible to volunteer for testing for STIs. Students visiting the SBHCs were usually females seeking reproductive health care and birth control prescriptions. From 1996 to 2003, 10,609 females were tested who were counted only once for each calendar year. Students could appear in more than 1 year. Between 1996 and 2003, 7463 unique female students were tested for CT. From these, there were 2915 females who had an initial test (positive or negative) and returned for at least 1 subsequent test for CT 30 to 365 days later. Of these, there were 897 students who tested positive initially and were then retested within 1 year; 236 of these were reinfected. Reinfection rates were analyzed for 1 year of follow-up after a positive chlamydia test.

Chlamydia reinfection was defined as a positive chlamydia NAAT result occurring between 30 and 365 days after an initial positive result. Nucleic acids from chlamydia can remain in infected individuals for up to 3 weeks after treatment, which can lead to positive NAAT tests immediately after successful treatment, so the 30-day limit was chosen as a conservative estimate of a new infection.[14]

Statistical analysis was performed by the Statistical Package for the Social Sciences for Windows (SPSS), version 11.0, Chicago, IL. χ^2 analyses were used to compare frequency data. Time to first repeat tests was calculated as the time between detection of the initial infection and the first test performed 30 days or more after detection.

Results

The overall prevalence for 10,609 females (unique females in each year studied) was 18.1% [95% confidence interval (CI) = 17.4-18.8%] and varied by year between 15.1% (95% CI = 13.1-17.1%) and 19.5% (95% CI = 17.8-21.2%) (Table 1). Total number of unduplicated females was 7463 (females could appear in more than 1 year). Numbers of females tested per year averaged 1326 (range, 512-2068) (Table 1). The total of positives for females was 1920; of those, 897 (46.7%), were rescreened.

There were 897 female students during the 8 years who tested positive for chlamydia and had at least 1 subsequent test between 30 and 365 days later. Mean time to first retest was 4.3

months (±3.4 months). Of the 897 infected female students retested following an initial infection, 236 had 1 or more subsequent positive tests for an overall cumulative incidence of reinfection of 26.3% (95% CI = 23.4-29.2%) (Table 1). By year, trends of incidence of reinfection for females who were tested again within 1 year varied by year but remained high (reinfection range of 14.3-38.9%) (Table 1).

Of the 236 female students who were reinfected, 135 (57.2%) received a second positive result directly following the first positive test. However, 101 (42.8%) had 1 or more negative test results between the initial positive and subsequent positive tests. Across school sites, the cumulative incidence of reinfection in female students ranged from 17.6% to 34.2% (Table 2). Young age at first infection was significantly associated with increased risk of subsequent infection (P <0.01). The risk of reinfection was highest in females aged 13 and under (38.9%, 95% CI = 23.0-54.8) (Table 3).

Discussion

Overall prevalences for chlamydia for unduplicated females from years 1996 to 2003 were over 15% each year. Trends have not decreased by year; the lowest prevalence was in 1999 at 15.1% and the highest prevalence was in 2002 at 19.5% (Table 1). Reasons for this are unclear; except that the cohorts are continually changing as students leave and new students come. The high prevalence may just reflect high community prevalence and the opportunity for transmission from unscreened males in both the schools and community. Fewer males are traditionally tested for chlamydia in our schools, but the prevalences are usually only slightly lower (8-10%) than for females (personal communication, Gerry Waterfield). The reasons for fewer males being tested in schools may include the fact that females more often seek reproductive health services, and adolescent males do not routinely seek health care unless they are symptomatic or are identified as a sexual contact to an infected female.[15-17] Provision of sports physicals by SBHCs may provide another venue that could provide opportunistic screening of both females and males for STIs.[18]

A significant limitation of this analysis is that the measure of incidence of reinfection presented is likely to be an overestimate of the true reinfection rate because it is limited to individuals who were positive once and then were retested subsequently. Since individuals are potentially more likely to have come back for a second test if they were symptomatic or suspected they were infected again, our estimate of reinfection is likely to be biased upward. Although this limitation exists, this approach to measuring incidence of reinfection has been employed by others.[11,19] Longitudinal cohort studies, which insure that all infected individuals get retested, would be required to determine the precise reinfection rate, however such studies are expensive and are potentially limited to small numbers of individuals. If one were to take the extreme case, where none of our remaining cohort was reinfected, the overall estimate of the incidence of reinfection would be 236/1920 or 12.3%. The true estimate is likely to lie somewhere between 26.3% and 12.3%. There is no way to correct for the bias in this analysis, but insight into what makes a student report for rescreening within 1 year may be instructive. As reported by the clinicians, students appear to be more likely to seek rescreening when they report having a new partner, which would put them at increased risk. It is also standard SBHC procedure that students are told to return for rescreening every 6 months and if they are infected, they are instructed to return for rescreening in 3 months. However there is no definitive method to know what prompted rescreening in this analysis.

We analyzed the data to ascertain repeat unique, individual infections in order to identify trends and reinfection incidence by age and school. The chlamydia incidence of reinfection rate in students from the 8 high and 3 middle schools in Baltimore was very high (26.3%) and not dissimilar from other earlier analyses of reinfection rates for females in some of these same

schools.[3] Our reinfection rates in Baltimore appeared to be much higher than those reported in earlier studies in other cities.[11,19-21] However, our methodology differed from that of other studies in that we looked at reinfection within 1 year, rather than the shorter time periods of 3 to 4 months or longer time periods of 3.4 years used by others.[11,21] Xu et al.,[11] using passive surveillance similar to that of our method, reported that among 32,698 women, 15% developed 1 or more repeat infections during a mean follow-up time of 3.4 years, while in those less than age 20 years, 6% were reinfected in 6 months, 11% by 1 year, and 17% by 2 years.[11] Whittington et al.[21] detected a reinfection rate of 7.1% at 1 month and 13.4% at 4 months. Additionally, a summary of published reinfection rates for chlamydia for 1- and 4-month periods reported a range from 5% to 13%.[22] Thus, comparisons of reinfection across studies are problematic with regard to timing of retesting. It has also been noted that studies relying on passive retrospective cohorts developed from health services data provide somewhat upwardly biased estimates of incidence of reinfection of STIs.[23] However, allowing for the lack of perfect cohort studies, the CDC recommends rescreening women who have a positive test in approximately 3 months in the latest treatment guidelines.[24]

Our trends for reinfection incidence in females, as measured by this analysis, have varied little over time; reinfection rates for 1 year ranged from 24.5% in 1996 to 21.6% in 2003. Participation in the school screening program in New Orleans demonstrated an incidence rate per 1000 person-months in students that were tested more than once during 3 years of screening of 4.3% (2.2, males; 7.1, females).[19] The differences from our analysis may be due to differences in timing of measurement of reinfection. Compared with our high reinfection incidence, their lower rate may also be due to the lower starting prevalences in these schools of 7.7% for females and 1.8% for males.[19] High-risk teens who were followed in adolescent clinics in Indianapolis over 3 years demonstrated initially high chlamydia rates (28.4%) and reinfection rates of 18% at visit 2 in 3 months, while at visit 3 in 9 months the reinfection rate for chlamydia was 20%, a rate not too dissimilar from our reinfection incidence of 25%, although it is difficult to compare results across studies.[8] The high reinfection incidence in our schools and in other cities requires more intense prevention interventions to lower these reinfection rates.

Since adolescents have the highest prevalences of chlamydia,[20] schools represent good opportunistic sites at which to perform screening programs. Similar to our study, others have reported substantial prevalences among high school students. Cohen et al.[25] reported that in 3 urban high schools in Louisiana, they found an overall prevalence of 6.5% (females 9.7% and males 4.0%) among 2849 consenting students out of 3278 enrolled. In Japan, the prevalence of asymptomatic chlamydia infection was reported to be 8.3% in 1004 high school students, indicating the universality of chlamydia infections and the need for implementation of sex education programs and behavioral interventions.[26]

Screening during sports physicals in SBHCs may present an additional opportunity to test more asymptomatic students.[26] In 1 study, 93% of athletes were asymptomatic; prevalence was 6.5% among females and 2.8% for males.[27] Not all high school screening studies have reported high chlamydia prevalences; of 283 female and 381 male asymptomatic students screened in San Francisco, a prevalence of 3.9% for females and 0.8% for males was demonstrated.[28] An example of high prevalence from screening in high schools was demonstrated in a comprehensive school screening program in Philadelphia, which reported an initial prevalence of 8.1% for females and 2.5% for males among 19,394 public high school students.[29]

The high reinfection rate among female school students in our analysis supports a local recommendation to screen adolescents frequently,[3] and especially if there is a history of a previous chlamydia infection, as recommended by the CDC.[24] Screening by urine-based tests makes rescreening easier to accomplish than obtaining cervical swabs. Young age of <20 years

for both males and females has been reported to be significantly associated with risk of STI reinfection in a large study of 64,463 patients attending sexually transmitted diseases clinics from 4 cities, indicating that emphasis for rescreening should be focused on adolescents.[30] Young age at first infection as detected in our study was also significantly associated with increased risk of reinfection; it may suggest that younger females may require more intensive interventions. Use of self-collected samples, such as urine and self-obtained vaginal swabs, which can be collected at home and mailed to a testing site, has been widely used in Europe to improve screening and rescreening.[31,32]

Future approval by the Food and Drug Administration for use of vaginal swabs collected at home may offer another way to encourage adolescent females to sample themselves more frequently, after initial screening in schools. Frequent rescreening appears to be urgently needed for adolescents, especially since teens often change sex partners and may have more than 1 partner.[33] Self-obtained vaginal swabs are highly accurate if tested by NAATs, are acceptable to women, and can be recommended as feasible for retesting adolescents for chlamydia.[34-39] Whether urines or self-obtained vaginal swabs are used, self-sampling may provide an optimal intervention to affect the epidemic of chlamydia in the United States. However, ways to improve rescreening of infected adolescents are needed and may include making advanced appointments, offering reminders through the school mail services, and providing home collection kits.

In summary, adolescent females attending SBHCs are at increased risk for reinfection with up to approximately 26% in Baltimore becoming reinfected with chlamydia within 1 year of their first documented infection. Intensive behavioral and educational interventions should be offered to adolescents. Our nurse practitioners are now providing single dose treatment at diagnosis, individualized risk reduction counseling, condoms with education, partner notification, and recommending rescreening of infected individuals at 3 months. Schools represent a logical forum for students to access health services. The installation of additional SBHCs should be encouraged, along with school-wide screening programs for sexually active students.[29]

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TABLE 1

Chlamydia trachomatis Infection Prevalence and Reinfection Rates Within 1 Year Among Female Adolescents Attending School-Based Health Centers, Who had Subsequent Tests Performed*

Year	Number Tested	Number Positive (%, 95% CI)	Initial Infections With Another Test	Repeat Infections at Rescreening	Repeat Infection Among Individuals Rescreened (%) (95% CI)
1996	512	82 (16.0, 12.8-19.2)	53	13	24.5 (12.9-36.1)
1997	841	159 (18.9, 16.3-21.5)	84	17	20.2 (11.6-28.8)
1998	1029	168 (16.3, 14.1-18.5)	63	9	14.3 (5.9-22.9)
1999	1198	181 (15.1, 13.1-17.1)	87	23	26.4 (17.2-35.6)
2000	1442	273 (18.9, 16.9-20.9)	127	40	31.5 (23.4-39.6)
2001	1597	289 (18.1, 16.2-20.0)	162	63	38.9 (31.4-46.1)
2002	2068	404 (19.5, 17.8-21.2)	196	44	22.4 (16.6-28.2)
2003	1922	364 (18.9, 17.2-20.6)	125	27	21.6 (14.4-28.8)
Total			897	236	26.3 (23.4-29.2)

*Individuals are counted only once per calendar year.

TABLE 2

Chlamydia trachomatis Infection Prevalence and Reinfection Rates for Females Within 1 Year Among Adolescents Attending School-Based Health Centers Who had Subsequent Tests Performed by School Site

Site ID	Number Tested	Number Positive (%, 95% CI)	Initial Infections With Another Test	Repeat Infections at Rescreening	Repeat Infection Among Individuals Rescreened (%) (95% CI)
A	718	205 (28.6, 25.3-31.9)	114	33	29.0 (20.7-37.3)
B	122	23 (18.9, 12.0-25.8)	7	2	28.6*
C	690	142 (20.6, 17.6-23.6)	76	18	23.7 (14.1-33.2)
D	372	82 (22.0, 17.8-26.2)	44	15	34.1 (20.1-48.1)
E	223	36 (16.1, 11.3-20.9)	21	5	23.8 (5.6-42.0)
F	614	132 (21.5, 18.3-24.7)	56	13	23.2 (12.2-34.2)
G	1158	222 (19.2, 16.9-21.5)	104	25	24.0 (15.8-32.2)
H	1099	287 (26.1, 23.5-28.7)	157	41	26.1 (19.2-33.0)
I	1085	287 (26.5, 23.9-29.1)	161	55	34.2 (26.9-41.5)
J	1101	248 (22.5, 20.0-25.0)	142	25	17.6 (11.3-23.9)
K	121	21 (17.4, 10.6-24.2)	11	3	27.3*
L	160	29 (18.1, 12.1-24.1)	4	1	25.0*
Total	7463		897	236	26.3

Counts are for unduplicated students.

*Confidence interval omitted due to inadequate sample size.

TABLE 3

Chlamydia trachomatis Reinfection Rates by Age Among Female Adolescents Attending School-Based Health Centers for Whom a Repeat Test was Performed, 1996-2003 (2 With Unknown Age Had No Reinfection)

Age (yr)	Initial Infection With Another Test	Repeat Infections at Rescreening	Repeat Infections Among Individuals Rescreened (%) (95% CI)
12-13	36	14	38.9 (23.0-54.8)
14	103	31	30.1 (21.3-38.9)
15	245	73	29.8 (24.1-35.5)
16	270	78	28.9 (23.5-34.3)
17	174	30	17.2 (11.6-22.8)
18	55	7	12.7 (3.9-21.5)
19-20	12	3	25.0*

P <0.01 (χ^2 test performed).

*Confidence interval omitted due to inadequate sample size.